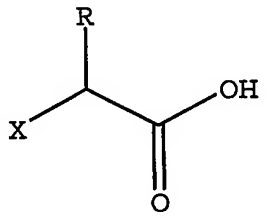
WE CLAIM:

1. A method for treating Huntington's disease comprising administering an effective amount of a NAALADase inhibitor to a mammal in need of such treatment.

2. The method of claim 1, wherein the NAALADase inhibitor is an acid containing a metal binding group.

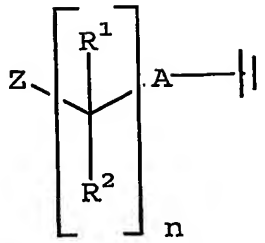
3. The method of claim 1, wherein the NAALADase inhibitor is a compound of formula I



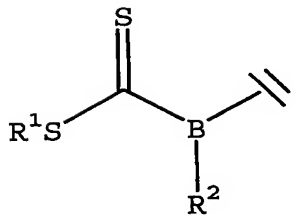
I

or an enantiomer or a pharmaceutically acceptable equivalent of said compound, wherein:

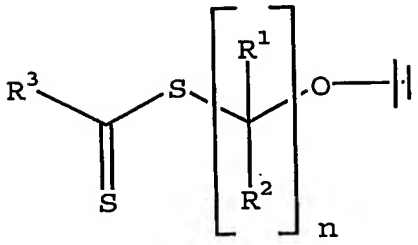
X is a moiety of formula II, III or IV



II



III



IV ;

Z is SH, SO_3H, SO_2H, SOH, $SO(NH)R^4$ or $S(NHR^4)_2R^5$;

B is N or CR^6;

A is O, S, CR^7R^8 or $(CR^7R^8)_mS$;

m and n are independently 0, 1, 2, 3 or 4;

R, R^1, R^2, R^3, R^4, R^5, R^6, R^7 and R^8 are independently hydrogen, C_1-C_9 alkyl, C_2-C_9 alkenyl, C_3-C_8 cycloalkyl, C_5-C_7 cycloalkenyl, Ar, hydroxy, carboxy, carbonyl, amino, cyano, isocyano, nitro, sulfonyl, sulfoxy, thio, thiocarbonyl, thiocyano, formanilido, thioformamido, sulfhydryl, halo, haloalkyl, trifluoromethyl or oxy, wherein said alkyl, alkenyl, cycloalkyl and cycloalkenyl are independently unsubstituted or substituted with one or more substituent(s); and

Ar is a carbocyclic or heterocyclic moiety, which is unsubstituted or substituted with one or more substituent(s);

provided that when X is a moiety of formula II and A is O, then n is 2, 3 or 4; when X is a moiety of formula II and A is S, then n is 2, 3 or 4; and when X is a moiety of formula II and A is $(CR^7R^8)_mS$, then n is 0, 2, 3 or 4.

4. The method of claim 3, wherein:

X is a moiety of formula II;

n is 0, 1, 2 or 3;

Z is SH, SO_3H, SO_2H, SOH or $S(NHR^4)_2R^5$; and

A is O, S or CR^7R^8.

5. The method of claim 4, wherein Z is SH.

6. The method of claim 5, wherein R is $-(CH_2)_2COOH$.

7. The method of claim 1, wherein the NAALADase inhibitor is selected from:

2-(2-sulfanylethyl)pentanedioic acid;

3-(2-sulfanylethyl)-1,3,5-pentanetricarboxylic acid;

2-(2-sulfanylpropyl)pentanedioic acid;

2-(2-sulfanylbutyl)pentanedioic acid;

2-(2-sulfanyl-2-phenylethyl)pentanedioic acid;

2-(2-sulfanylhexyl)pentanedioic acid;

2-(2-sulfanyl-1-methylethyl)pentanedioic acid;

2-[1-(sulfanylmethyl)propyl]pentanedioic acid;

2-(3-sulfanylpentyl)pentanedioic acid;

2-(3-sulfanylpropyl)pentanedioic acid;

2-(3-sulfanyl-2-methylpropyl)pentanedioic acid;

2-(3-sulfanyl-2-phenylpropyl)pentanedioic acid;

2-(3-sulfanylbutyl)pentanedioic acid;

2-[3-sulfanyl-2-(phenylmethyl)propyl]pentanedioic acid;

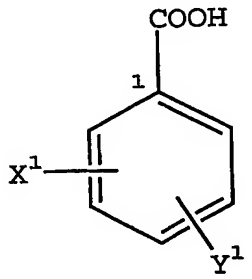
2-[2-(sulfanylmethyl)butyl]pentanedioic acid;

2-[2-(sulfanylmethyl)pentyl]pentanedioic acid;

2-(3-sulfanyl-4-methylpentyl)pentanedioic acid; and

enantiomers and pharmaceutically acceptable equivalents.

8. The method of claim 1, wherein the NAALADase inhibitor is a compound of formula V



V

or an enantiomer or a pharmaceutically acceptable equivalent of said compound, wherein:

X^1 is $-W-Z^1$;

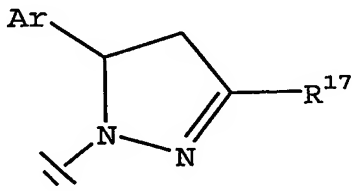
W is a bond or a linking group;

Z^1 is a terminal group; and

Y^1 is -COOH oriented *meta* or *para* relative to C-1.

9. The method of claim 8, wherein:

X^1 is $-(CR^9R^{10})_nNH(CR^{11}R^{12})_mCOOH$, $-PO(OH)OR^{14}$, $-(CR^9R^{10})_nP(O)(OH)R^{14}$, $-NH-(CR^{11}R^{12})_m$-heteroaryl, $-NH(P(O)(R^{15})OH)$, $-(CR^9R^{10})_nNH(P(O)(OH)R^{15})$, $-CON(R^{14})(OH)$, $-(CR^9CR^{10})_nCON(R^{14})(OH)$, $-(CR^9R^{10})_nSH$, $-O(CR^{11}R^{12})_mSH$, $-SO_2NH$-aryl, $-N(C=O)-CH_2(C=O)$-aryl, $-SO_2NH$-aryl, $-N(C=O)-CH_2(C=O)$-aryl or -O-aryl, wherein aryl in -O-aryl is substituted by at least one of nitro, carboxy or



wherein X^1 is oriented *meta* or *para* relative to C-1;

Ar is a carbocyclic or heterocyclic moiety, which is unsubstituted or substituted with one or more substituent(s);

m and n are independently 1-3, provided that when X^1 is $-O(CR^{11}R^{12})_mSH$, then m is 2 or 3;

R^9, R^{10}, R^{11}, R^{12}, R^{14}, R^{15} and R^{17} are independently hydrogen, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, aryl,

heteroaryl, carbocycle, heterocycle, halo, hydroxy, sulfhydryl, nitro, amino or C_1-C_6 alkoxy, wherein said alkyl, alkenyl, alkynyl, aryl, heteroaryl, carbocycle, heterocycle and alkoxy are independently unsubstituted or substituted with one or more substituent(s); and

Y^1 is -COOH oriented *meta* or *para* relative to C-1.

10. The method of claim 8, wherein X^1 is oriented *ortho* relative to C-1, and Y^1 is oriented *para* relative to X^1 and *meta* relative to C-1.

11. The method of claim 10, wherein W is a bond, and Z^1 is $-CO_2H$, -OH, $-NO_2$, $-C(O)(NHR^{15})$, $-SR^{15}$, $-COR^{15}$ or $-NH(CH_2R^{15})$, and R^{15} is an aryl or a heteroaryl wherein said aryl and heteroaryl are independently unsubstituted or substituted with one or more alkyl, nitro or carboxy group(s).

12. The method of claim 10, wherein W is $-(CH_2)_n-$ and n is 1-3, and Z^1 is -SH.

13. The method of claim 8, wherein the linking groups are selected from divalent hydrocarbon chains, ethers, sulfides and amines, wherein the hydrocarbon chains, whether alone or part of ethers, sulfides, and/or amines, may be saturated or unsaturated, straight or branched, open or closed, unsubstituted or substituted with one or more substituents.

14. The method of claim 13, wherein the one or more substituents are independently selected from C_1-C_6 alkoxy, C_2-C_6 alkenyloxy, phenoxy, benzyloxy, hydroxy, carboxy, carbamido, carbamoyl, carbamyl, carbonyl, carbozoyl, amino, hydroxyamino, formamido, formyl, guanyl, cyano, cyanoamino, isocyano, isocyanato, diazo, azido, hydrazino, triazano, nitro, nitroso, isonitroso, nitrosamino, imino, nitrilo, isonitrilo, nitrosimino, oxo, C_1-C_6 alkylthio, sulfamino, sulfamoyl, sulfeno, sulfhydryl, sulfinyl, sulfo, sulfonyl, sulfoxy, thiocarboxy, thiocyano, isothiocyano, thioformamido, halo, haloalkyl, chlorosyl, chloryl, perchloryl, trifluoromethyl, iodosyl, iodyl, phosphino, phosphinyl, phospho, phosphono, arsino, selanyl, diselanyl, siloxy, silyl and silylene groups.

15. The method of claim 8, wherein W is a bond, $-(CR^9R^{10})_n-$, $-(CR^9R^{10})_nO(CR^{11}R^{12})_m-$, $-(CR^9R^{10})_nS(CR^{11}R^{12})_m-$ or $-(CR^9R^{10})_nNR^{13}(CR^{11}R^{12})_m-$, wherein m and n are independently 0-9, and R^9, R^{10}, R^{11}, R^{12} and R^{13} are independently hydrogen, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_6-C_{14} aryl, heteroaryl, C_6-C_{14} carbocycle, heterocycle, halo, hydroxy, sulfhydryl, nitro, amino or C_1-C_6 alkoxy, and said alkyl, alkenyl, alkynyl, aryl, heteroaryl, carbocycle, heterocycle and alkoxy are independently unsubstituted or substituted with one or more substituents.

16. The method of claim 15, wherein R^9, R^{10}, R^{11}, R^{12} and R^{13} are each hydrogen and the total number of carbon atoms in W is 2-6.

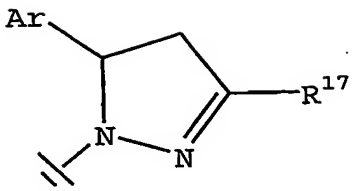
17. The method of claim 8, wherein Z^1 is a metal binding group.

18. The method of claim 8, wherein Z^1 is -COOH, $-COR^{14}$, $-OR^{14}$, $-CF_3$, -CN, -F, -Cl, -Br, -I, -NO, $-NO_2$, $-C(O)(NR^{14}OR^{15})$, $-C(O)(NR^{14}PO_3H_2)$, $-C(O)(NR^{14}R^{15})$, =NOH, $-NR^{14}(P(O)(R^{15})OH)$, $=NR^{14}$, $-N=NR^{14}$, $-N(R^{14})CN$, $-NR^{14}(CR^{15}R^{16})_pCOOH$, $-NR^{14}(CO)NR^{15}R^{16}$, $-NR^{14}(COOR^{15})$, $-NR^{14}(CO)R^{15}$, $-NR^{14}(OR^{15})$, $-NR^{14}R^{15}$, $-NR^{14}(SO_2R^{15})$, $-O(CO)R^{14}$, $-OR^{14}$, $-SO_2(OR^{14})$, $-SO_2(NR^{14}R^{15})$, $-SO_2R^{14}$, $-SO_3R^{14}$, $-SNR^{14}(OR^{15})$, $-S(NR^{14}R^{15})$, $-SR^{14}$, $-SSR^{14}$, $-P(O)(OH)OR^{14}$, $-P(O)(OH)R^{14}$ or $-PR^{14}R^{15}$, wherein p is 0-6, and R^{14}, R^{15} and R^{16} are independently hydrogen, C_1-C_9 alkyl, C_2-C_9 alkenyl, C_2-C_9 alkynyl, C_6-C_{14} aryl, heteroaryl, C_6-C_{14} carbocycle, heterocycle, halo, hydroxy, sulfhydryl, nitro, amino or C_1-C_9 alkoxy, and said alkyl, alkenyl, alkynyl, aryl, heteroaryl, carbocycle, heterocycle and alkoxy are independently unsubstituted or substituted with one or more substituents.

19. The method of claim 18, wherein Z^1 is $-NH(CR^{15}R^{16})_pCOOH$, $-PO(OH)OR^{14}$, $-PO(OH)R^{14}$, $-NR^{14}(P(O)(R^{15})OH)$, $-CON(R^{14})(OH)$ or -SH.

20. The method of claim 8, wherein

X^1 is $-(CR^9R^{10})_nNH(CR^{11}R^{12})_mCOOH$, $-PO(OH)OR^{14}$, $-(CR^9R^{10})_nP(O)(OH)R^{14}$, $-NH-(CR^{11}R^{12})_m$-heteroaryl, $-NH(P(O)(R^{15})OH)$, $-(CR^9R^{10})_nNH(P(O)(OH)R^{15})$, $-CON(R^{14})(OH)$, $-(CR^9CR^{10})_nCON(R^{14})(OH)$, $-(CR^9R^{10})_nSH$, $-O(CR^{11}R^{12})_mSH$, $-SO_2NH$-aryl, $-N(C=O)-CH_2(C=O)$-aryl, $-SO_2NH$-aryl, $-N(C=O)-CH_2(C=O)$-aryl, or -O-aryl wherein aryl in -O-aryl is substituted by at least one of nitro, carboxy or



wherein X^1 is oriented *meta* or *para* relative to C-1;

Ar is a carbocyclic or heterocyclic moiety, which is unsubstituted or substituted with one or more substituent(s);

m and n are independently 1-3, provided that when X^1 is $-O(CR^{11}R^{12})_mSH$, then m is 2 or 3;

R^9, R^{10}, R^{11}, R^{12}, R^{14}, R^{15} and R^{17} are independently hydrogen, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, aryl, heteroaryl, carbocycle, heterocycle, halo, hydroxy, sulfhydryl, nitro, amino or C_1-C_6 alkoxy, wherein said alkyl, alkenyl, alkynyl, aryl, heteroaryl, carbocycle, heterocycle and alkoxy are independently unsubstituted or substituted with one or more substituents; and

Y^1 is -COOH oriented *meta* or *para* relative to C-1.

21. The method of claim 20, wherein X^1 is $-PO(OH)OR^{14}$ or $-(CR^9R^{10})_nP(O)(OH)OR^{14}$, and R^{14} is not H or methyl.

22. The method of claim 20, wherein X^1 is $-NH(P(O)(R^{15})OH$ or $-(CR^9R^{10})_nNH(P(O)(OH)R^{15})$, and R^{15} is not benzyl unsubstituted or substituted with amino.

23. The method of claim 20, wherein X^1 is $-CON(R^{14})(OH)$, and R^{14} is not H or methyl.

24. The method of claim 8, wherein X^1 is oriented *meta* relative to C-1, and Y^1 is oriented *ortho* relative to X^1 and *para* relative to C-1.

25. The method of claim 24, wherein W is a bond, $-(CH_2)_n-NH-(CH_2)_m-$ or $-(CH_2)_n-$; m is 1-3; n is 0-3; and Z^1 is $-CO_2H$, $-NO_2$, $-NH_2$, $-SO_3H$, halo, C_5-C_6 heteroaryl, carboxyphenylthio, or mono- or di-carboxyphenylsulfonyl.

26. The method of claim 8, wherein X^1 is oriented *meta* relative to C-1, and Y^1 is oriented *meta* relative to X^1 and *meta* relative to C-1.

27. The method of claim 26, wherein W is a bond, $-(CH_2)_n-$ or $-O(CH_2)_m-$ and m and n are independently 0-3, and Z^1 is $-SO_3H$, $-NO_2$, $-NH_2$, $-CO_2H$, -OH, $-PO_3H$, -CO(NHOH), -SH or an optionally substituted phenyl wherein one or more substituents are selected from nitro and carboxy.

28. The method of claim 26, wherein W is $-(CH_2)_nNH(CH_2)_m-$ and m and n are independently 0-3, and Z^1 is $-CO_2H$ or C_5-C_6 heteroaryl.

29. The method of claim 26, wherein W is $-(CH_2)_n-$ wherein n is 0-3, and (a) Z^1 is a heteroaryl that is unsubstituted or substituted with an aryl that is unsubstituted or substituted with one or more C_1-C_3 alkyl, halo, nitro or hydroxy group(s), or (b) Z^1 is $-SO_2(NHR^{16})$ or

-NH(COR^{16}), wherein R^{16} is an optionally substituted C_1-C_3 alkyl wherein one or more substituents are selected from oxo, phenyl, and substituted phenyl; and R^{16} may also be selected from an aryl that is unsubstituted or substituted with one or more nitro, amino, halo or hydroxy group(s).

30. The method of claim 1, wherein the NAALADase inhibitor is selected from:

2-[(4-carboxyphenyl)sulfonyl]-1,4-benzene-dicarboxylic acid;

2-[(2,5-dicarboxyphenyl)sulfonyl]-1,4-benzene-dicarboxylic acid;

1,2,4-benzenetricarboxylic acid;

2-[(2-carboxyphenyl)thio]-1,4-benzenedicarboxylic acid;

2-nitro-1,4-benzenedicarboxylic acid;

2-bromo-1,4-benzenedicarboxylic acid;

2-amino-1,4-benzenedicarboxylic acid;

2-sulfoterephthalic acid, monosodium salt;

2-carboxymethyl-1,4-benzenedicarboxylic acid;

2-[(2-furanylmethyl)-amino]-1,4-benzenedicarboxylic acid;

2-[(carboxymethyl)amino]-1,4-benzenedicarboxylic acid;

4-(4-nitrobenzoyl)-1,3-benzenedicarboxylic acid;

4-[4-(2,4-dicarboxybenzoyl)phenoxy]-1,2-benzene-dicarboxylic acid;

4-[4-(2,4-dicarboxybenzoyl)phenoxy]-1,3-benzene-dicarboxylic acid;

4-[[(2,4,6-trimethylphenyl)amino]carbonyl]-1,3-benzenedicarboxylic acid;

4-nitro-1,3-benzenedicarboxylic acid;

4-[(1-naphthalenylamino)-carbonyl]-1,3-benzene-dicarboxylic acid;

1,2,4-benzenetricarboxylic acid;

4-[(2-carboxyphenyl)thio]-1,3-benzenedicarboxylic acid;

4-[3-[[3-(2,4-dicarboxyphenoxy)propyl]dithio]-propoxy]-1,3-benzenedicarboxylic acid;

4-hydroxy-1,3-benzenedicarboxylic acid;

4-[(2-furanylmethyl)amino]-1,3-benzenedicarboxylic acid;

4-(2-mercaptoethyl)-1,3-benzenedicarboxylic acid;

5-[4,5-dihydro-5-(4-hydroxyphenyl)-3-phenyl-1H-pyrazol-1-yl]-1,3-benzenedicarboxylic acid;

5-(4,5-dihydro-3-methyl-5-phenyl-1H-pyrazol-1-yl)-1,3-benzenedicarboxylic acid;

5-[[(4-chloro-3-nitrophenyl)amino]sulfonyl]-1,3-benzenedicarboxylic acid;

5-[[[4-chloro-3-[[3-(2-methoxyphenyl)-1,3-dioxopropyl]amino]phenyl]amino]sulfonyl-1,3-benzenedicarboxylic acid;

5-[[3-[4-(acetylamino)phenyl]-1,3-dioxopropyl]amino]-1,3-benzenedicarboxylic acid;

5-acetylamino-1,3-benzenedicarboxylic acid;

5-[[(1-hydroxy-2-naphthalenyl)carbonyl]-methylamino]-1,3-benzenedicarboxylic acid;

5-(4-carboxy-2-nitrophenoxy)-1,3-benzenedicarboxylic acid;

5-sulfo-1,3-benzenedicarboxylic acid;

5-nitro-1,3-benzenedicarboxylic acid;

5-amino-1,3-benzenedicarboxylic acid;

1,3,5-benzenetricarboxylic acid;

5-[[(3-amino-4-chlorophenyl)amino]sulfonyl]-1,3-benzenedicarboxylic acid;

5-(3-mercaptopropoxy)-1,3-benzenedicarboxylic acid;

5-hydroxy-1,3-benzenedicarboxylic acid;

5-(2-mercaptoethoxy)-1,3-benzenedicarboxylic acid;

5-[(hydroxyamino)carbonyl]-1,3-benzenedicarboxylic acid;

5-phosphono-1,3-benzenedicarboxylic acid;

5-mercaptomethyl-1,3-benzenedicarboxylic acid;

5-phosphonomethyl-1,3-benzenedicarboxylic acid;

5-[[(carboxymethyl)amino]-methyl]-1,3-benzene-dicarboxylic acid;

5-[(carboxymethyl)amino]-1,3-benzenedicarboxylic acid;

5-[[(2-furanylmethyl)amino]-methyl]-1,3-benzene-dicarboxylic acid;

5-[2-(hydroxyamino)-2-oxoethyl]-1,3-benzene-dicarboxylic acid;

5-(2-mercaptoethyl)-1,3-benzenedicarboxylic acid; and

enantiomers and pharmaceutically acceptable equivalents.

31. A method for treating Huntington's disease comprising administering an effective amount of a compound selected from:

2-[(4-carboxyphenyl)sulfonyl]-1,4-benzene-dicarboxylic acid;

2-[(2,5-dicarboxyphenyl)sulfonyl]-1,4-benzene-dicarboxylic acid;

1,2,4-benzenetricarboxylic acid;

2-[(2-carboxyphenyl)thio]-1,4-benzenedicarboxylic acid;

2-nitro-1,4-benzenedicarboxylic acid;

2-bromo-1,4-benzenedicarboxylic acid;

2-amino-1,4-benzenedicarboxylic acid;

2-sulfoterephthalic acid, monosodium salt;

2-carboxymethyl-1,4-benzenedicarboxylic acid;

2-[(2-furanylmethyl)-amino]-1,4-benzenedicarboxylic acid;

2-[(carboxymethyl)amino]-1,4-benzenedicarboxylic acid;

4-(4-nitrobenzoyl)-1,3-benzenedicarboxylic acid;

4-[4-(2,4-dicarboxybenzoyl)phenoxy]-1,2-benzenedicarboxylic acid;

4-[[(2,4,6-trimethylphenyl)amino]carbonyl]-1,3-benzenedicarboxylic acid;

4-nitro-1,3-benzenedicarboxylic acid;

4-[(1-naphthalenylamino)-carbonyl]-1,3-benzenedicarboxylic acid;

1,2,4-benzenetricarboxylic acid;

4-[(2-carboxyphenyl)thio]-1,3-benzenedicarboxylic acid;

4-[3-[[3-(2,4-dicarboxyphenoxy)propyl]dithio]-propoxy]-1,3-benzenedicarboxylic acid;

4-hydroxy-1,3-benzenedicarboxylic acid;

4-[(2-furanylmethyl)amino]-1,3-benzenedicarboxylic acid;

4-(2-mercaptoethyl)-1,3-benzenedicarboxylic acid;

5-[4,5-dihydro-5-(4-hydroxyphenyl)-3-phenyl-1H-pyrazol-1-yl]-1,3-benzenedicarboxylic acid;

5-(4,5-dihydro-3-methyl-5-phenyl-1H-pyrazol-1-yl)-1,3-benzenedicarboxylic acid;

5-[[(4-chloro-3-nitrophenyl)amino]sulfonyl]-1,3-benzenedicarboxylic acid;

5-[[[4-chloro-3-[[3-(2-methoxyphenyl)-1,3-dioxopropyl]amino]phenyl]amino]sulfonyl-1,3-benzenedicarboxylic acid;

5-[[3-[4-(acetylamino)phenyl]-1,3-dioxopropyl]amino]-1,3-benzenedicarboxylic acid;

5-acetylamino-1,3-benzenedicarboxylic acid;

5-[[(1-hydroxy-2-naphthalenyl)carbonyl]-methylamino]-1,3-benzenedicarboxylic acid;

5-(4-carboxy-2-nitrophenoxy)-1,3-benzenedicarboxylic acid;

5-sulfo-1,3-benzenedicarboxylic acid;

5-nitro-1,3-benzenedicarboxylic acid;

5-amino-1,3-benzenedicarboxylic acid;

1,3,5-benzenetricarboxylic acid;

5-[[(3-amino-4-chlorophenyl)amino]sulfonyl]-1,3-benzenedicarboxylic acid;

5-(3-mercaptopropoxy)-1,3-benzenedicarboxylic acid;

5-hydroxy-1,3-benzenedicarboxylic acid;

5-(2-mercaptoethoxy)-1,3-benzenedicarboxylic acid;

5-[(hydroxyamino)carbonyl]-1,3-benzenedicarboxylic acid;

5-phosphono-1,3-benzenedicarboxylic acid;

5-mercaptomethyl-1,3-benzenedicarboxylic acid;

5-phosphonomethyl-1,3-benzenedicarboxylic acid;

5-[[(carboxymethyl)amino]-methyl]-1,3-benzene-dicarboxylic acid;

5-[(carboxymethyl)amino]-1,3-benzenedicarboxylic acid;

5-[[(2-furanylmethyl)amino]-methyl]-1,3-benzene-dicarboxylic acid;

5-[2-(hydroxyamino)-2-oxoethyl]-1,3-benzene-dicarboxylic acid;

5-(2-mercaptoethyl)-1,3-benzenedicarboxylic acid; and

enantiomers and pharmaceutically acceptable equivalents.

32. A pharmaceutical composition comprising:

(i) an effective amount of a NAALADase inhibitor for treating Huntington's disease; and

(ii) a pharmaceutically acceptable carrier.

33. A method of making a pharmaceutical composition comprising mixing an effective amount of a NAALADase inhibitor for treating Huntington's disease and a pharmaceutically acceptable carrier.